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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,040	06/21/2005	Thomas Schmehl	080618-0576	4643

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EXAMINER	
SHOMER, ISAAC	

ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,040	SCHMEHL ET AL.	
	Examiner	Art Unit	
	ISAAC SHOMER	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-25 and 27-52* is/are pending in the application.

4a) Of the above claim(s) *15,16,19,20 and 27-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14, 17, 18, 21-25, and 50-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 2 August 2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 11-14, 17, 21, 22, 25, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (US Patent 5,049,388).

Knight et al. (hereafter referred to as Knight) teaches liposome aerosol droplets comprising a drug, as of Knight, abstract. Said droplets are introduced to the respiratory tract of a patient by mixing with air and oxygen enriched air, as of Knight, column 8 lines 55-58, and as such would deliver drugs to the lungs. The lipids used in said liposome may include sphingomyelin and dipalmitoylphosphatidylcholine (abbreviated as DPPC), as of Knight, column 8 lines 31-35, and sterols such as cholesterol to increase the stability of the bilayers, as of Knight, column 8 lines 39-41. In one example, cholesterol was present at one half the phosphatidylcholine concentration (by mass), as of Knight,

column 12 lines 13-17 and Table 4. Liposomes may be multilamellar, as of Knight, column 8 lines 21-23. Knight teaches that any type of aerosol nebulizer may be used which reduces the size of the liposomes to the desired range and produces an aqueous aerosol, as of Knight, column 10 lines 35-39.

The specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables specifically DPPC, cholesterol, and sphingomyelin, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007) (quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007).

The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients specifically DPPC, cholesterol, and sphingomyelin, from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Knight teaches a liposome comprising cholesterol at half the concentration of phosphatidylcholine, but does not specifically teach liposome comprising cholesterol at half the concentration of DPPC. However, Knight teaches an example wherein cholesterol was present at one half the phosphatidylcholine concentration (by mass), as of Knight, column 12 lines 13-17 and Table 4. As DPPC is a known phosphatidylcholine and is taught by Knight, the skilled artisan would have been motivated to have made a liposome with cholesterol at half the concentration of DPPC for predictable administration by aerosol with a reasonable expectation of success because Knight teaches that this relative amount of cholesterol to phosphatidylcholine is useful for preparing the liposomes.

While Knight does not teach that upon administration to the lungs, 50% to 80% of the liposomes stay intact, the skilled artisan would have expected that liposomes administered by the method of Knight would have stayed intact upon pulmonary administration. This is because the liposomes of Knight contain cholesterol at a concentration in the range of the claimed concentration. As sterols are taught to increase the stability of the bilayers (as of Knight, column 8 lines 39-41), the skilled

artisan would have expected that the presence of cholesterol would have cause the liposomes to be stable and to have remained intact upon respiratory administration.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (US Patent 5,049,388) as applied to claims 11-14, 17, 21, 22, 25, and 52 above and further in view of Modi (US Patent 6,193,997).

Knight teaches administration of a liposomal composition comprising a drug to the respiratory tract. See the above rejection. Said liposome may include sphingomyelin, as of Knight, column 8 lines 31-35.

Knight does not teach the weight percentage of sphingomyelin.

Modi teaches a liposome pharmaceutical formulation with multilamellar vesicles, as of Modi, abstract, first sentence. Said composition may be used for pulmonary drug delivery, as of Modi, column 1 lines 9-11. Said liposome may contain sphingomyelin as a phospholipid, as of Modi, abstract, seventh line from bottom. Said composition may contain a phospholipid between 1% and 10% by mass, as of Modi, abstract, second to last sentence.

It would have been prima facie obvious for one of ordinary skill in the art to have formulated sphingomyelin at a concentration of 1% to 10% in the liposome used by Knight. The skilled artisan would have been motivated to do so because sphingomyelin is a known phospholipid for liposome formulation, and is taught by Modi to be predictably effective at a concentration 1% to 10% for a liposome used for pulmonary access with a reasonable expectation of success.

A concentration of 1% to 10% of sphingomyelin does not read on the claims but overlaps with the claimed range. While the prior art does not disclose the exact claimed values, but does overlap: in such instances even a slight overlap in range establishes a *prima facie* case of obviousness. In re Peterson, 65 USPQ2d 1379, 1382 (Fed. Cir. 2003).

Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (US Patent 5,049,388) as applied to claims 11-14, 17, 21, 22, 25, and 52 above and further in view of Nagata et al. (US 2001/0055610).

Knight teaches administration of a liposomal composition comprising a drug to the respiratory tract. See the above rejection. Knight teaches administration via nebulizer, as of Knight, column 10 lines 10-11.

Knight does not teach an air-jet nebulizer or an ultrasonic nebulizer.

Nagata et al. (hereafter referred to as Nagata) teaches a liposomal formulation for administration via inhalation, wherein inhalation occurs using a jet nebulizer, a metered dose inhaler, a dry powder inhaler, or an ultrasonic nebulizer, as of Nagata, abstract, and further comprising a biologically active substance. Said liposome may include dipalmitoyl phosphatidylcholine (DPPC) and sphingomyelin, as of Nagata, paragraph 0035, and cholesterol as a membrane stabilizer, as of Nagata, paragraph 0038.

It would have been prima facie obvious for one of ordinary skill in the art to have used the nebulizer of Nagata to have administered the liposomes of Knight. The skilled

artisan would have been motivated to do so because the methods used by Nagata would have predictably administered liposomes comprising a drug via inhalation with a reasonable expectation of success. Generally, it is *prima facie* obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended use. See MPEP 2144.07.

Claims 50 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al. (US Patent 5,049,388) as applied to claims 11-14, 17, 21, 22, 25, and 52 above and further in view of Max et al. (European Journal of Pediatrics, Vol. 158, Suppl 1, 1999, pp. S23-S26).

Knight teaches administration of a liposomal composition comprising a drug to the respiratory tract. See the above rejection. Knight teaches a wide variety of drugs to be administered, as of Knight, columns 6 and 7, Table 1.

Knight does not teach a prostacyclin.

Max et al. (hereafter referred to as Max) teaches the administration of prostacyclin to treat pulmonary hypertension via various routes including aerosolized delivery (i.e. pulmonary delivery), as of Max, page S23, abstract.

It would have been prima facie obvious for one of ordinary skill in the art to have used prostacyclin as the drug to be delivered in the liposomal delivery method of Knight. The skilled artisan would have been motivated to have done so because administration of prostacyclin to the lungs via inhalation is suggested as of Max. As such, the skilled artisan would have been motivated to have predictably used prostacyclin as the specific

drug in the method of Knight with a reasonable expectation of success. Generally, it is prima facie obvious to select a known material for incorporation into a composition, based on its recognized suitability for its intended use. See MPEP 2144.07.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ISAAC SHOMER/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612